Primary peritoneal clear cell carcinoma - A diagnostic dilemma

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ABSTRACT

Peritoneum is a site for both primary and secondary tumors. Clear cell carcinoma of the peritoneum is an extremely rare primary tumor. The diagnosis of primary peritoneal tumors is based on the gynecology oncology group criteria, originally described for primary adenocarcinoma of the peritoneum. A 55-year-old female presented with non-specific pain in the lower abdomen of 1-month duration. Contrast-enhanced computed tomography findings of the abdomen were suggestive of suspected neoplastic mass most likely arising from the left ovary. Pre-operative serum cancer antigen-125 levels were 252 U/ml. Upon exploratory laparotomy, a hard nodular mass appearing to arise from anterior abdominal wall (15 × 12 cm) was found in the left iliac fossa. Histopathological diagnosis of primary peritoneal clear cell carcinoma was made and immunohistochemistry was performed for confirmation.

Key words: *Cancer antigen-125, Clear cell carcinoma, Immunohistochemistry (estrogen receptors, cytokeratin-7), Primary peritoneal carcinoma*

Peritoneum is a site for both primary and secondary tumors. Primary peritoneal clear cell carcinoma (PPCC) is very rare and very few cases have been reported till date [1]. With its histomorphological resemblance to malignant mesothelioma, serous carcinoma, metastatic adenocarcinoma and clear cell carcinoma, it is a great diagnostic challenge to the pathologists. Further due to paucity of the information available on biological behavior, pathogenesis, and management plan and treatment outcome, it remains a clinical challenge yet to be explored. We report a case of PPCC to add to the existing knowledge on the clinicopathological feature of this rare tumor.

CASE REPORT

A 55-year-old female presented with non-specific pain in the lower abdomen for 1 month. She was a known case of hypothyroidism on a regular dose of 100 mg thyroxin once a day. There was no other significant present or past history. On examination, she was conscious, oriented with stable vitals, and unremarkable general examination findings. Per abdomen examination revealed a hard, nodular mass appearing to arise from the anterior abdominal wall in the left iliac fossa. Systemic examination revealed no significant finding.

Hematological investigations revealed neutrophilic leukocytosis with total leukocyte count of 15,000/mm^3 and differential leukocyte count of 90% neutrophils, 08% lymphocytes, and 2% monocytes. Rest of the investigations including liver and renal function tests were within normal limits. Ultrasonography of lower abdomen revealed uterus and bilateral ovaries of normal size along with a large tumor on the left side. Contrast-enhanced computed tomography (CECT) findings of the abdomen were suggestive of suspected neoplastic mass most likely arising from left ovary and involving anterior wall with ipsilateral pelvic lymphadenopathy. A provisional diagnosis of ovarian neoplasm was made on the basis of CECT findings and patient was planned for surgery. Preoperatively serum cancer antigen-125 (CA) was 252 U/ml.

Upon exploratory laparotomy, a hard nodular mass arising from the anterior abdominal wall was found in the region of left iliac fossa rather than from the left ovary. Primary cytoreductive surgery which included excision of abdominal wall mass, total abdominal hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic lymphadectomy was performed. On gross examination (Fig. 1), abdominal wall mass was hard, globular, and measured 15 × 13 × 4 cm. Outer surface was bosselated and showed congested blood vessels. On cut open, yellowish watery fluid oozed out. Cut surface showed a solid area measuring 10 × 8 cm along with multiple cystic spaces and numerous, soft, friable, grayish-white papillary excrescences. Wall thickness of the cystic spaces varied from 0.3 to 0.5 cm. Uterus and bilateral adnexa were of normal size and appeared uninvolved grossly. Representative sections were taken from formalin fixed specimen, processed as per routine protocol, stained with hematoxylin, and eosin stain; and observed microscopically. Relevant immunohistochemical stains were ordered for representative sections.

Microscopy of the abdominal mass showed a tumor composed of cells arranged in tubuloglandular, papillary, or occasionally in solid pattern with cells displaying high N:C ratio, pleomorphic

vesicular nuclei, prominent eosinophilic nucleoli, and clear to eosinophilic cytoplasm. A hobnail arrangement of the cells was also noted. Focal areas of necrosis and calcification were noted. 5/10 HPF mitotic figures and apoptotic bodies were seen. Mild chronic inflammatory infiltrate was noticed in the surrounding connective tissue stroma (Figs. 2 and 3). Left external iliac lymph nodes (3/3) and left pelvic lymph nodes (6/8) showed metastatic deposits while right pelvic lymph nodes (0/5) were negative for tumor infiltration. Uterus and bilateral adenexa were free of tumor infiltration and showed no other significant finding. Based on the above described morphology, provisional diagnosis of PPCC was made with primary peritoneal serous carcinoma (PPSC) and malignant mesothelioma as closest differential diagnosis. Immunohistochemistry (IHC) confirmed the diagnosis of PPCC as the tumor cells were positive for cytokeratin-7 (CK), CA-125, epithelial membrane antigen, and vimentin and negative for estrogen receptors (ER), Wilm's tumour-1 (WT-1), CK-20, CK-5/6, and calretinin (Figs. 4-6).

The immediate post-operative follow-up was uneventful with good recovery and following which the patient was discharged.

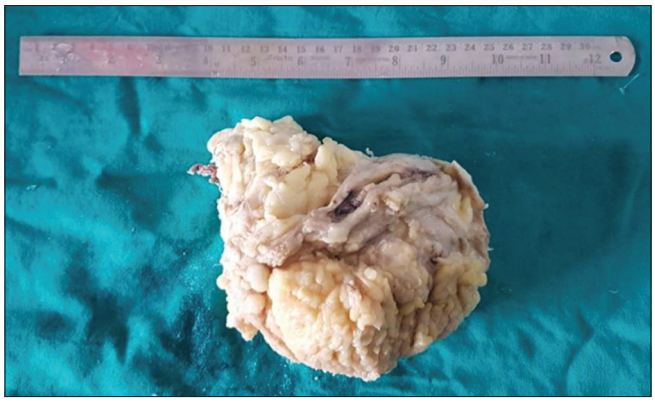

Figure 1: Globular mass with bosselated outer surface

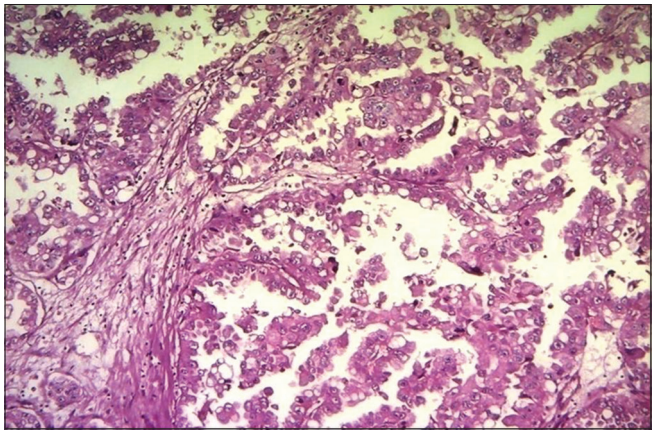

Figure 2: Papillary configuration and hobnail arrangement of cells

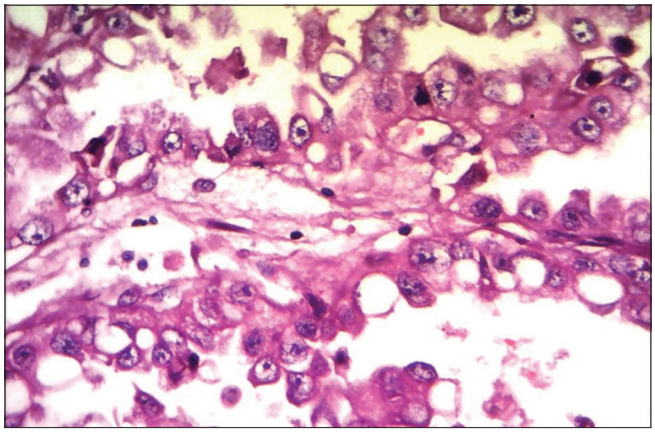

Figure 3: Cells displaying high N:C ratio, pleomorphic vesicular nucleus with prominent nucleolus and clear to eosinophilic cytoplasm

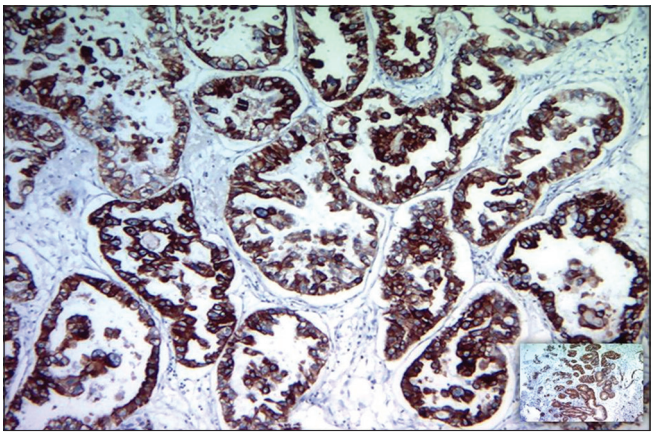

Figure 4: Immunostain for cytokeratin-7 (positive), inset - positive control

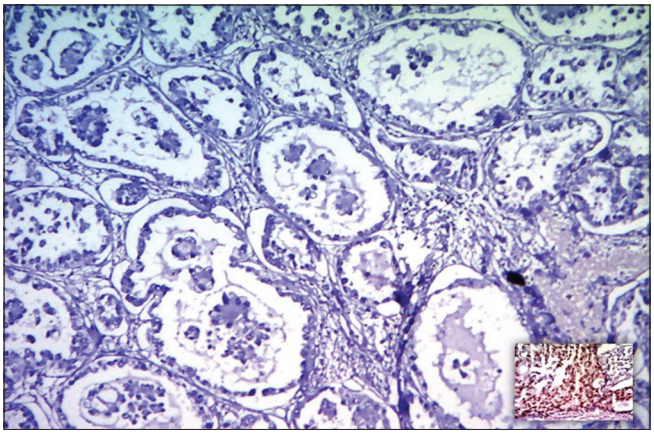

Figure 5: Immunostain for estrogen receptor (negative), inset - positive control

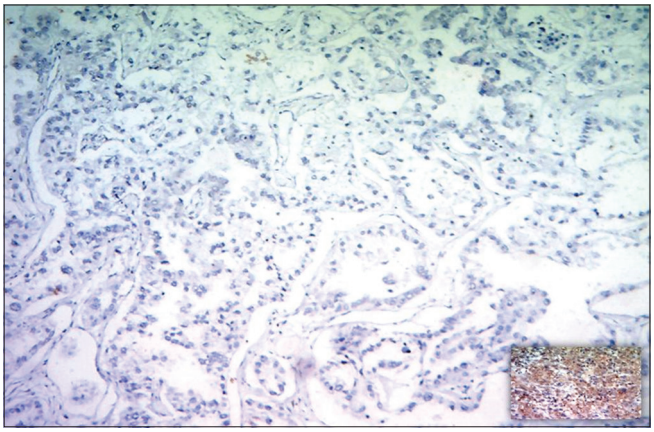

Figure 6: Immunostain for calretinin (negative), inset - positive control

The patient was lost to further follow-up; however, interviewed telephonically the patient had received 6 cycles of chemotherapy (carboplatin and paclitaxel) every 3 weeks for 6 weeks. Post-chemotherapy positron emission tomography/CECT did not reveal any residual tumor and the patient has not developed any other complaint since then.

DISCUSSION

PPCC is extremely rare, accounting for approximately 3% of primary peritoneal carcinomas, with an incidence of 0.46/100,000 cases [2] and the first case to be reported among all the diagnosed malignant cases in the past 10 years at our institute, thus supporting the rarity of its occurrence. Most of the cases of PPCC reported till date have affected females in the age group of 45-67 years, as also seen in the present case [1].

Abdominal distention and pain with or without ascites are the most frequently encountered clinical presentations [1]. Concurrent uterine pathologies reported in most of the cases were endometriosis, uterine adenocarcinoma, and endometrial hyperplasia [1]. In this case, no associated uterine pathology was identified. The diagnosis of primary peritoneal tumor is based on the gynecology oncology group criteria, originally described for primary adenocarcinoma of the peritoneum [3]. Diagnosis of PPCC is often difficult preoperatively and on routine histopathological examination, as morphologically it closely resembles to malignant mesothelioma of peritoneum, PPSC, metastatic peritoneal carcinomatosis, and peritoneal psammocarcinoma [1].

Definitive diagnosis requires extensive IHC. Malignant mesothelioma can be differentiated from PPCC due to its positivity for calretinin and CK5/6, which are negative in PPCC [1]. Besides, mesothelioma has male preponderance and an associated history of long-term asbestos exposure, while PPCC has been mostly reported in females [4]. PPSC is typically positive for CK-7, ER, CA-125, and WT-1 [1]; thus, differentiating it from PPCC [1]. Peritoneal serous psammocarcinoma has more numerous psammoma bodies >80% of epithelial nests, less aggressive cytology, absent or moderate nuclear atypia, and rare mitosis as compared to PPCC [5]. PPCC are histologically similar to ovarian carcinomas and are believed to behave similarly [6]. Debulking surgery and chemotherapy remains the mainstay of the treatment and radiotherapy appears to be effective in local control [6]. Mortality remains high in patients with PPCC, with a median survival of approximately 24 months and 5 years survival rate of 18% [7].

CONCLUSION

The current report presents a case of PPCC in a 55-year-old female. Due to its significant rarity, diagnostic challenges and sparsity of literature available on its biological behavior and treatment outcome, it is imperative to explore further, various clinicopathological aspects of this rare tumor through long-term follow-up of the patient to provide substantial information necessary for appropriate patient management.

REFERENCES

1. Insabato L, Natella V, Somma A, Persico M, Camera L, Losito NS, et al. Primary peritoneal clear cell carcinoma versus ovarian carcinoma versus malignant transformation of endometriosis: A vexing issue. Int J Surg Pathol. 2015;23(3):211-6.
2. Goodman MT, Shvetsov YB. Rapidly increasing incidence of papillary serous carcinoma of the peritoneum in the United States: Fact or artifact? Int J Cancer. 2009;124(9):2231-5.
3. Alvarez JV, Gomez MM, Prats MD, Agoreeta MA, Cajal JM, Lopez JI, et al. Extra ovarian primary peritoneal carcinoma. A case report. Rev Esp Patol. 2007;40:47-52.
4. Heda K, Indushekar B, Pachori G, Sharma A. Primary peritoneal serous carcinoma: A diagnostic dilemma of pelvic epithelial neoplasms. Clin Cancer Investig J. 2015;4(4):551-4.
5. Yun WS, Bae JM. Primary peritoneal serous carcinoma, an extremely rare malignancy: A case report and review of the literature. Oncol Lett. 2016;11(6):4063-5.
6. Johnson SB, Prisciandaro JI, Zhou J, Hadley SW, Reynolds RK, Jolly S. Primary peritoneal clear cell carcinoma treated with IMRT and interstitial HDR brachytherapy: A case report. J Appl Clin Med Phys. 2014;15(1):4520.
7. Kim YM, Lee YM, Lee SH, Lee DW, Kim KH. Primary peritoneal carcinoma initially presenting as atypical cervical lymphadenopathy. Case Rep Oncol. 2015;8(2):246-50.

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